

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY


(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 11 AUG 2005

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Applicant's or agent's file reference 00701		FOR FURTHER ACTION		See Form PCT/IPEA/416
International application No. PCT/EP2004/050350		International filing date (day/month/year) 23.03.2004		Priority date (day/month/year) 11.04.2003
International Patent Classification (IPC) or national classification and IPC C07D493/04, A61P35/00				
Applicant PHARMACIA ITALIA S.P.A. et al.				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in Item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input checked="" type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand 06.09.2004		Date of completion of this report 09.08.2005		
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer Stroeter, T Telephone No. +49 89 2399- 8088		



**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2004/050350

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-63 as originally filed

Claims, Numbers

1-25 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2004/050350

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees, the applicant has:
- ☐ restricted the claims.
 - ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☒ neither restricted nor paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
- ☐ complied with.
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-22 .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-22
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-22
Industrial applicability (IA)	Yes: Claims	1-22
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

**INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)**

International application No.

PCT/EP2004/050350

Re Item IV

Lack of unity of invention

The present application does not fulfil the requirements of claims Rule 13.1 PCT because it claims the following separate inventions:

1. Claims 1-22:

Claims directed to compounds for use as scaffolds for combinatorial libraries and a chemical library of certain compounds deducted from said scaffolds.

2. Claims 23-25:

Claims directed to pharmacological active compounds (defined via a screening method)

By comparison of claims 1-22 with claims 23-25 it must be stated that the requirements of unity of invention *a priori* are not met for the following reasons: There is no common problem underlying both groups of inventions, since a library itself must have a technical feature which represents a contribution over the prior art. This contribution necessarily differs from the one associated with individual congeners of a library since active and inactive structures are encompassed by a library of compounds. Thus the inventive step for a library is associated with a specific effect for this entity as such, whereas inventiveness for a single compound in the present case relates to a certain pharmacological activity (here: e.g. anti-tumor activity).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Subject-matter of the independent claims

The present application is directed to certain glucose-related bicyclic structures which serve as scaffolds for combinatorial libraries in search for protein kinase/polymerase/protease inhibitors useful in the treatment of tumors.

Claimed are:

- said scaffolds (independent claims 1 and 6)
- methods for their preparation (independent claims 7-9)
- a chemical library of compound deducted from said scaffolds (indep. claim 11)
- a screening method applied on this library (independent claim 22)
- compounds identified by this method (independent claim 23)
- use of the identified compound(s) for the preparation of a medicament (independent claim 24)

2 Prior art documents

Reference is made to the following documents. The given numbering will be adhered to in the rest of the procedure:

- D1: WO 97/34906 A (UNIV PRINCETON) 25 September 1997
- D2: WO 00/20428 A (MASSACHUSETTS INST TECHNOLOGY) 13 April 2000
- D3: BORMAN S: "COMBINATORIAL CARBOHYDRATES. PROSPECTS ARE LOOKING SWEET FOR USE OF SUGAR-BASED COMBINATORIAL LIBRARIES TO FIND NOVEL BIOACTIVE SUBSTANCES" CHEMICAL AND ENGINEERING NEWS, AMERICAN CHEMICAL SOCIETY. COLUMBUS, US, vol. 76, no. 29, 20 July 1998, pages 49-52
- D4: CHIAPPE C ET AL: "An efficient stereoselective synthesis of enantiomerically pure aziridine derivatives of allyl beta-d-glucopyranosides asymmetrically induced by a glucide moiety" TETRAHEDRON: ASYMMETRY, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 9, no. 22, 27 November 1998, pages 4079-4088
- D5: HARAGUCHI, KAZUHIRO ET AL: "The synthesis of octosyl nucleosides based on intramolecular oxyselenation of a conjugated diene The synthesis of octosyl nucleosides based on intramolecular oxyselenation of a conjugated diene (studies directed toward the total synthesis of azaspiracid via construction of the C1-C19 carbon backbone" TETRAHEDRON LETTERS , 39(31), 5517-5520 CODEN: TELEAY

3 Novelty (Article 33(2) PCT)

The glucose derivatives of prior art documents D1-D3 lack the present fused tetrahydrofuran moiety whereas documents D4, D5 relate to compounds having the same parental oxabicyclic ring system but differ in the sugar-related substitution of said ring system. Therefore the compounds of formula (I), (II), (XXVII) and (XXVIII) are novel rendering claims 1-22 novel.

4 Inventive step (Article 33(3) PCT)

In view of the prior art also related to the provision of chemical libraries of glucose-related compounds (see e.g. D1, D2 or D3) the present technical problem underlying the present invention (claims 1-22) can be seen as to provide a further library. The preparation and provision of libraries for screening purposes *per se* is considered to be obvious. An inventive step can only be acknowledged if the library itself - and not certain library components - has an unexpected effect, use or property.

Consequently the libraries claimed in claims 11-21 and the screening method of claim 22 as well as the scaffold compounds claimed in claims 1-10 are not inventive.

5 Industrial applicability (Article 33(4) PCT)

The subject-matter of the present claims 1-22 is in accordance with the requirements of Article 33(4) PCT.